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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

MAIL DATE	DELIVERY MODE
07/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/754,997	SALBAUM, J. MICHAEL	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *1-8 and 16-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-15 and 20-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/1/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/1/07 has been entered.

2. Claims 1-42 are pending.

3. Claims 1-8 and 16-19 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claims 9-15 and 20-42 are under examination as they read on an isolated nucleic acid molecule of SEQ ID NO: 1 encoding Nope polypeptide of SEQ ID NO: 2 and SEQ ID NOs: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23 and oligonucleotides 300-325, 325-350 and 300-350 as the species.

5. The status identifier of claims 11 and 15 is wrong, i.e., "Withdrawn". It should be either "Previously presented or Original". Correction is required.

6. The disclosure stands objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Page 25, line 22 contains embedded hyperlinks and/or other forms of browser-executable code which are impermissible and require deletion.

7. Applicant's IDS, filed 6/1/07, is acknowledged.

8. 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

9. Claims 9-15 and 20-42 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the same reasons set forth in the previous Office Action mailed 9/23/05 and 5/4/06.

Further, Applicant provided Vielmetter et al (1994, IDS ref) to support his position. Vielmetter et al teach that based on the amino acid sequence similarities, neogenin is closely related to the human tumor suppressor molecule DCC (deleted in colorectal cancer). Further, Vielmetter et al teach that these parallel suggest that neogenin, like DCC, is functionally involved in the

transition from cell proliferation to terminal differentiation of specific cell types (abstract in particular). However, a recent publication by Xie et al (JBC, 281(5):2605-2611, 2006) teach that neurite-1 regulate phosphatidylinositol signaling in cortical neurons is mediated by DCC, but not neogenin (see abstract). Importantly, Xie et al conclude that the data have indicated a role of DCC, but not neogenin in netrin-1 induced PIP2 hydrolysis, supporting the notion that different functions could be mediated by DCC and neogenin (see page 2609, 2nd col., last ¶).

This supports the Examiner's position that structural similarity is not predictive of functional similarity. Functional relatedness is not credible in the face of evidence in the art that structurally related polypeptides in the Ig-like families are frequently dissimilar functionally. The members of the family have different biological activities, but there is no evidence that the claimed compounds would share any one of those different activities. That is, no activity is known to be common to all members of DCC protein.

Applicant's arguments, filed 3/23/06, have been fully considered, but have not been found convincing.

Applicant maintains that the specification teaches a substantial and specific utility and is clearly distinguishable from the EST's at issue in *In re fisher*. The *In re Fisher* decision makes it clear that the threshold for utility of a DNA sequence is the identification of a function for the underlying protein-encoding genes. Analysis of the Nope sequence revealed that the protein encoded by the Nope nucleic acid sequence contains four IG domains and five fibronectin-type domains, has structural similarity to DCC, Punc and NCAM, and most closely resembles cell adhesion molecules (page 46, lines 8-17). The specification further teaches the function of these structurally related proteins as axonal guidance receptors (page 49, lines 22, to page 50, line 7). The specification also teaches the developmental expression of Nope, including its expression in cells of the nervous system (Example II, pages 46-48, in particular page 47, line 27, to page 48m line 16). The specification clearly provides and explicit teaching of a specific, substantial and credible utility of the Nope polynucleotide in that it encodes a protein expressed in the nervous system and that functions as an axonal guidance receptor. Further, the specification teaches that Nope is expressed in the developing mouse embryo in the notochord, in developing muscle tissues and in the developing nervous system (page 47, line 10, to page 48, line 16). Nope expression is concentrated in the ventricular zone in the brain and in the hippocampus, the piriform contex, thalamic nucleic and foliae of the cerebellum of adult brain (page 48, lines 3-16). The specification teaches that Nope functions in cells of the nervous system that arise late in gestation (page 48, lines 8-11). Applicant maintains that the specification provides a clear ând credible teaching of a functional role of Nope in neuronal development. Further Applicant concludes that the claimed nucleic acids encoding Nope are correlated in the specification with well known structural motifs, proteins will known function, and tissue expression consistent with the function.

Many genes expressed in diseased tissues have nothing whatsoever to do with the disease and are not targets for drug development. For example, actin and histone genes are expressed in

diseased tissues; they are constitutively expressed in all tissues. These are not suitable targets for drug development, since disruption of these genes would kill the patient. The specification failed to confirm a correlation that claimed SEQ ID NO:2 encoding SEQ ID NO: 1 is a causal factor in such nervous system.

Further, no single effect of the disclosed NOPE is ascribed to the polypeptide encoded by the claimed polynucleotide. Note that while the specification produces the full-length polypeptide encoded by the claimed polynucleotide, recombinantly, no biological or biochemical activity is established for the full length polypeptide or any of the fragments thereof. As such, further research would be required to identify or research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved would be required.

Furthermore, neither the instant specification or the art of record identifies even a single disease or disorder which has been shown to be associated with the NOPE proteins of the instant invention. It has not been shown that Nope is differentially expressed in any disease or disorder, the encoded polypeptide cannot be employed in a diagnostic capacity. Further, the "NOPE proteins" of the instant invention has not been shown to be associated with a particular physiological process which an artisan would wish to manipulate for clinical effect by the administration of the encoded protein or an agonist or antagonist thereof. Because an artisan does not know if an agonist-induced response by the encoded protein enhances or inhibits nervous system diseases.

Applicant submits that the IG and fibronectin domains are well known structural motifs. Applicant submits that he is unaware of the basis for the assertion in the Office Action on page 4, that proteins with very similar sequence fold up differently and requested that the Examiner provide evidence that proteins with very similar sequences fold differently. Applicant submits that the immunoglobulin and fibronectin domains are well haracterized structural domains present on cell surface receptors and diffusible ligands that function as binding domains. A subgroup of the immunoglobulin superfamily has been associated with migration and guidance of axonal growth cones.

The Examiner notes the evidence was provided by the Examiner in the previous Office Action. That is Alexandersson lecture titled Pairwise sequence alignment (http://www.fcc.chalmers.se/~marina/files/BioII_Pairwise_2003.pdf, 2003), as evidence that proteins with very similar sequence fold up differently (see page 1, in particular). Further, sequence similarity does not always means similar folding and function. Applicant did not dispute the teachings of Alexandersson but maintains that he is unaware of such basis. Further, the four immunoglobulin domain and five FnIII repeats of Nope shares only 45% amino acid sequence similarity with mouse Punc. Further, the cytoplasmic domains of NOPE and mouse Punc do not share amino acid sequence similarity. Further, the rejection sets forth that, among related polypeptides in the Ig and FnIII families, structural similarity is not predictive of functional similarity. The immunoglobulin superfamily (IgSF) is a heterogenic group of proteins built on a common fold, called the Ig fold, which is a sandwich of two beta sheets. Although members of the IgSF share a similar Ig fold, they differ in their tissue distribution, amino acid

composition, and biological role. Rougon et al (Annu Rev Neurosci. 2003;26:207-38. 2003) teach that immunoglobulin-superfamily (IgSF) proteins are implicated in diverse steps of brain development, including neuronal migration, axon pathfinding, target recognition and synapse formation, as well as in the maintenance and function of neuronal networks in the adult. Rougon *et al* illustrate that the complexity of IgSF protein function results from various different levels of regulation including regulation of gene expression, protein localization, and protein interactions. Functional relatedness is not credible in the face of evidence in the art that structurally related polypeptides in the Ig-like families are frequently dissimilar functionally. The members of the family have different biological activities, but there is no evidence that the claimed compounds would share any one of those different activities. That is, no activity is known to be common to all members of DCC protein.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 9-15 and 20-42 stand also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Further, the specification does not provide sufficient enablement for how to make any nucleic acid molecule encoding a Nope polypeptide of SEQ ID NO: 2 and having a "Nope polypeptide activity" or "modification" of the encoding nucleic acid sequence or a "modification" of SEQ ID NO:1 in claims 9-10; a kit comprising one or more Nope oligonucleotides consisting of the anti-sense strand of Nope oligonucleotides of SEQ ID NO: 1 in claims 20-24. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action mailed 9/23/05 and 5/4/06.

Applicant's arguments, filed 3/23/06, have been fully considered, but have not been found convincing.

Applicant included the arguments for this rejection with the utility rejection above. The Examiner's position is the same as above.

12. Claims 9-10 and 14 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed 9/23/05.

Applicant's arguments, filed 3/23/06, have been fully considered, but have not been found convincing.

Applicant submits that the specification teaches that a modification of a nucleic acid can include one or several nucleotide additions, deletions or substitutions with respect to a reference sequence, including a substantially the same nucleotide sequence that can hybridize under moderately stringent or higher stringency conditions (page 9, lines 16-30). The specification also teaches various stringency conditions. Applicant concludes that the specification provides sufficient description and guidance for the claimed nucleic acid molecules and modifications thereof.

However, neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the genus. That is, the specification provides neither a representative number of species (modified Nope) to describe the claimed genus, nor does it provide a description of structural features that are common to species (of modified Nope). The specification provides no structural description of Nope other than ones specifically exemplified; in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed modifications looks like. The specification's disclosure is inadequate to describe the claimed genus of a modification of the encoding Nope nucleic acid sequence.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

July 20, 2007

Maher Haddad

Maher Haddad, Ph.D.
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TC 1600